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Amendment Dated June 29, 2006 Reply to Office Action of May 17, 2006

<u>Amendments to the Claims:</u> This listing of claims will replace all prior versions, and listings, of claims in the application

Listing of Claims:

- 1. (Currently amended) An aqueous formulation comprising, on a gram per ml (w/v) basis:
 - a. a block copolymer;
 - b. a polyethylene glycol (PEG); and
 - e. 1-2 % 2,6-diisopropylphenol;
 - d. propylene glycol; and

e. water and up to 15% excipients, said excipients consisting essentially of, on a gram per ml total formulation basis, up to 6% polyethylene glycol (PEG), up to 10% of a block copolymer, namely poloxamer 188, and optionally, one or more pH modifiers, stabilizers, or tonicity modifiers, said formulation comprising an aqueous solution clear to the naked eye.

- 2-9. (Canceled)
- 10. (Canceled)
- 11. (Amended) The formulation of claim $\frac{10}{1}$, wherein the total amount of said block copolymer is from about 5% to about 10% (w/v) of said formulation.
- 12. (Amended) The formulation of claim $\frac{11}{2}$, wherein the total amount of said block copolymer is from about 6% to 8% (w/v) of said formulation.
 - 13. (Canceled)
 - 14. (Canceled)
 - 15. (Canceled)
 - 16. (Canceled)
 - 17. (Canceled)
 - 18 (Canceled)
 - 19. (Canceled)

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20. (Amended) The formulation of claim $\frac{19}{1}$, wherein the amount of 2,6-diisopropylphenol is about 1% (w/v) of said formulation.

- 21. (Canceled)
- 22. (Canceled)
- 23. (Amended) The formulation of claim $\frac{221}{2}$, wherein the total amount of PEG is less than about 5% (w/v) of said formulation.
- 24. (Amended) The formulation of claim $\frac{221}{2}$, wherein the total amount of PEG is between about 2% and about 6% (w/v) of said formulation.
- 25. (Previously presented) The formulation of claim 24 wherein the PEG is between about 2% and 4% of said formulation.
- 26. (Amended) The formulation of claim $\frac{251}{2}$, wherein the total amount of PEG is between about 3 and 4% (w/v) of said formulation.
- 27. (Previously presented) The formulation of claim 1, wherein said PEG is selected from the group consisting of PEG-300, PEG-400, PEG-600, PEG-800, and PEG-1000.
- 28. (Previously presented) The formulation of claim 27, wherein said PEG is PEG-400.
- 29. (Amended) The formulation of claim 1, wherein the amount of said excipients include propylene glycol and said propylene glycol is not more than 5% (w/v) of said formulation.
- 30. (Amended) The formulation of claim 29, wherein the amount of propylene glycol is not more than 2% (w/v) of said formulation.
- 31. (Amended) The formulation of claim 30, wherein the amount of propylene glycol is $1\% \text{ or } \underline{\text{to}} \ 2\% \ (\text{w/v})$ of said formulation.

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32. (Amended) The formulation of claim 1, wherein said formulation further comprises excipients include citric acid or a salt thereof.

- 33. (Amended) The formulation of claim 32, wherein formulation comprises the concentration of said citric acid at a concentration between about in said formulation is in the range of from 2.5 and to 15 mM.
- 34. (Previously presented) The formulation of claim 32, wherein said formulation comprises citric acid in an amount of about 2 mg/ml.
- 35. (Amended) The formulation of claim 1, wherein said formulation further comprises said excipients include an antimicrobial agent.
- 36. (Previously presented) The formulation of claim 35, wherein said antimicrobial agent is selected from the group consisting of disodium edetate, metabisulfate, benzyl alcohol, cysteine or a salt thereof, EDTA.
- 37. (Previously presented) The formulation of claim 36, wherein said antimicrobial agent is benzyl alcohol in the amount of up to 0.5% (w/v) of said formulation.

38. (Canceled)

- 39. (Amended) The formulation of claim $\frac{3828}{28}$, wherein poloxamer 188 is present in an amount between 6 and 8% (w/v) of said formulation; PEG-400 is present in an amount between 2 and 4% (w/v) of said formulation; and the excipients include propylene glycol is present in an amount not greater than 2% (w/v) of said formulation; and 2,6 disopropylphenol is present in an amount between 1 and 2% (w/v) of said formulation.
- 40. (Amended) The formulation of claim $\underline{2838}$, wherein poloxamer 188 is present in an amount of about 8% (w/v) of said formulation; PEG-400 is present in an amount of about 4% (w/v) of said formulation; propylene glycol is present \underline{as}

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an excipient in an amount of about 1% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation.

- 41. (Amended) The formulation of claim $\underline{2838}$, wherein poloxamer 188 is present in an amount of about 8% (w/v) of said formulation; PEG-400 is present in an amount of about 3% (w/v) of said formulation; propylene glycol is present \underline{as} an excipient and in an amount of about 1% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation.
- 42. (Amended) The formulation of claim $\underline{2838}$, wherein poloxamer 188 is present in an amount of about 7% (w/v) of said formulation; PEG-400 is present in an amount of about 4% (w/v) of said formulation; propylene glycol is present \underline{as} \underline{an} $\underline{excipient}$ in an amount of about 1% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation.
- 43. (Amended) The formulation of claim $\underline{2838}$, wherein poloxamer 188 is present in an amount of about 7% (w/v) of said formulation; PEG-400 is present in an amount of about 3% (w/v) of said formulation; propylene glycol is present, as an excipient, in an amount of about 1% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation.
- 44. (Amended) The formulation of claim $\underline{2838}$, wherein poloxamer 188 is present in an amount of about 6% (w/v) of said formulation; PEG-400 is present in an amount of about 4% (w/v) of said formulation; propylene glycol is present, as an excipient, in an amount of about 1% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation.
- 45. (Amended) The formulation of claim <u>2838</u>, wherein poloxamer 188 is present in an amount of about 6% (w/v) of said formulation; PEG-400 is present in an amount of about 4% (w/v) of said formulation; propylene glycol is present, <u>as an excipient</u>, in an amount of about 2% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation.

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- 46. (Amended) The formulation of claim $\underline{2838}$, wherein poloxamer 188 is present in an amount of about 6% (w/v) of said formulation; PEG-400 is present in an amount of about 6% (w/v) of said formulation; propylene glycol is present, as an excipient, in an amount of about 1% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation.
- 47. (Amended) The formulation of claim 2838, wherein poloxamer 188 is present in an amount of about 8% (w/v) of said formulation; PEG-400 is present in an amount of about 2% (w/v) of said formulation; propylene glycol is present, as an excipient, in an amount of about 1% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation.
- 48. (Amended) The formulation of claim $\underline{2838}$, wherein poloxamer 188 is present in an amount of about 7% (w/v) of said formulation; PEG-400 is present in an amount of about 2% (w/v) of said formulation; propylene glycol is present, as an excipient, in an amount of about 1% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation.
 - 49. (Amended) An aqueous formulation, comprising:
 - a. a block copolymer in an amount of less than about 10% (w/v) of said formulation;
 - b. a polyethylene glycol in an amount of between about 2% and 4% (w/v) of said formulation
 - $\epsilon \underline{a}$. 2,6-diisopropylphenol; and
 - db. water, and
 - c. up to 15% (w/v) excipients, said excipients comprising a block copolymer in an amount of less than about 10% (w/v) of said formulation, a polyethylene glycol in an amount of between about 2% and 4% (w/v) of said formulation, and optionally, one or more pH modifiers, stabilizers, or tonicity modifiers, and the formulation includes no other glycol or alcohol and is transparent.
- 50. (Amended) The formulation of claim 49, wherein said block copolymer is poloxamer 188, present in an amount of between about 5% to about

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9% (w/v) of said formulation; and said polyethylene glycol is PEG-400, present in an amount of between about 2% and 4% (w/v) of said formulation.

51. (Previously presented) The formulation of claim 50, wherein poloxamer 188 is present in an amount of about 8% (w/v) of said formulation; PEG-400 is present in an amount of about 4% (w/v) of said formulation; and 2,6-diisopropylphenol in an amount of about 1% (w/v) of said formulation, wherein said formulation is substantially free of propylene glycol.

52. (Previously presented) The formulation of claim 50, wherein poloxamer 188 is present in an amount of about 8% (w/v) of said formulation; PEG-400 is present in an amount of about 3% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation, wherein said formulation is substantially free of propylene glycol.

53. (Previously presented) The formulation of claim 50, wherein poloxamer 188 is present in an amount of about 7% (w/v) of said formulation; PEG-400 is present in an amount of about 4% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation, wherein said formulation is substantially free of propylene glycol.

54. (Previously presented) The formulation of claim 50, wherein poloxamer 188 is present in an amount of about 7% (w/v) of said formulation; PEG-400 is present in an amount of about 3% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation, wherein said formulation is substantially free of propylene glycol.

55. (Previously presented) The formulation of claim 50, wherein poloxamer 188 is present in an amount of about 9% (w/v) of said formulation; PEG-400 is present in an amount of about 2% (w/v) of said formulation; and 2,6-diisopropylphenol is present in an amount of about 1% (w/v) of said formulation.

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56. (Previously presented) The formulation of claim 50, wherein poloxamer 188 is present in an amount of 8% (w/v) of said formulation; and PEG-400 is present in an amount of 2% (w/v) of said formulation.

- 57. (Previously presented) The formulation of claim 50, wherein poloxamer 188 is present in an amount of 7% (w/v) of said formulation; and PEG-400 is present in an amount of 2% (w/v) of said formulation.
- 58. (Amended) The formulation of claim 49, further comprising, in the excipient portion thereof, citric acid or a salt thereof.
- 59. (Previously presented) The formulation of claim 58, wherein said formulation comprises citric acid at a concentration between about 2.5 and 10 mM.
- 60. (Amended) The formulation of claim 49, further comprising, in the excipient portion thereof, an antimicrobial agent.
- 61. (Previously presented) The formulation of claim 60, where said antimicrobial agent is benzyl alcohol.
- 62. (Amended) The formulation of claim 1 or claim 49, wherein said formulation further comprises, in the excipient portion thereof, polysorbate.
- 63. (Amended) The formulation of claim 62, wherein 2,6-diisopropylphenol is present in an amount of about 0.5 to about 2.4 percent (w/v) of said formulation; further including in the excipient portion thereof, polyoxyethylene 20 sorbitan monooleate is present, in an amount of about 0.5 to about 15 percent (w/v) of said formulation; propylene glycol is present in an amount of about 0.5 to about 15 percent (w/v) of said formulation; PEG-400 is present in an amount of about 1 to about 20 percent (w/v) of said formulation; and poloxamer 188 is present in an amount of about 2 to about 15 percent (w/v) of said formulation.
- 64. (Previously presented) The composition of claim 1 or claim 49, wherein said block copolymer is purified poloxamer, wherein said purified poloxamer has a

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polydispersity value of between about 5 and 1, about 4 and 1, about 3 and 1, about 2 and 1, or about 1.1 and 1.

65. (Canceled)

- 66. (Amended) An aqueous formulation, consisting essentially of:
- a. a block copolymer in an amount of less than about 10% (w/v) of said formulation;
 - b. a polyethylene glycol in an amount of between about 2% and about 6% (w/v) of said formulation;
 - c. 2,6-diisopropylphenol;
 - d. water;
 - e. optionally citric acid or a salt thereof; and
 - f. optionally an antimicrobial agent

said components a, b, e, and f comprising excipients of said formulation, said excipients, in total, not exceeding 15% (w/v) of said formulation, said formulation being clear to the naked eye.

- 67. (Amended) The formulation of claim 66, wherein said formulation citric acid or a salt thereof comprises citric acid.
- 68. (Amended) The formulation of claim 66, wherein the excipients of said formulation comprises include an antimicrobial agent.
 - 69. (Canceled)
 - 70. (Canceled)
- 71. (Amended) A lipid-free microemulsion, comprising consisting essentially of:
 - a. a block copolymer, namely poloxamer 188;
 - b. a polyethylene glycol (PEG);
 - c. 2,6-diisopropylphenol;
 - d. propylene glycol; and
 - e. water,

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said components a, b, and d comprising excipients and said excipients not exceeding 15% (w/v) of said formulation, said microemulsion being lipid-free and clear.

- 72. (Amended) An aqueous formulation, comprising consisting essentially of:
 - a. a block copolymer, <u>namely poloxamer 188</u> in an amount of less than about 10% (w/v) of said formulation;
 - b. a polyethylene glycol in an amount of between about 2% and 4% (w/v) of said formulation;
 - c. 2,6-diisopropylphenol; and
 - d. water;

said components a and b comprising no more than 15% (w/v) of said formulation, wherein said formulation has an average particle size of less than about 65 nanometers.

- 73. (Amended) A method of inducing or maintaining anesthesia in a mammal, comprising administering to said mammal an amount of a formulation, as claimed in any one of claims 1, 49, 75 or 66, effective to induce or maintain anesthesia.
- 74. (Amended) A multi-use container, comprising the formulation as claimed in any one of claims 1, 49, or 66, or 75.
- 75. (New) A formulation comprising a injectable anesthetic solution, including citric acid and an antimicrobial agent as optional components, said formulation including no more than 15% excipients and comprising, in addition to said optional components, a clear aqueous composition selected from the group consisting of:
 - a. 1% propofol, 9% poloxamer 188, 2% PEG 400, and water;
 - b. 1% propofol, 8% poloxamer 188, 4% PEG 400, and water;
 - c. 1% propofol, 8% poloxamer 188, 4% PEG 400, 1% propylene glycol, and water;

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d. 1% propofol, 8% poloxamer 188, 3% PEG 400, and water;

- e. 1% propofol, 8% poloxamer 188, 3% PEG 400, 1% propylene glycol, and water;
- f. 1% propofol, 7% poloxamer 188, 4% PEG 400, and water; and
- g. 1% propofol, 7% poloxamer 188, 4% PEG 400, 1% propylene glycol, and water.
- 76. (New) The formulation of claims 1 or 49 wherein said pH modifiers are selected from the group consisting of sodium hydroxide, potassium hydroxide, and hydrochloric acid.
- 77. (New) An aqueous formulation, comprising:
 - a. 2,6-diisopropylphenol; and
 - b. water, and
- c. up to 15% (w/v) excipients, said excipients comprising, on a gram per mL total formulation basis, 8% poloxamer 188, 3% polyethylene glycol 400, 1% propylene glycol, 0.2% citric acid monohydrate, a preservative, and sodium hydroxide, wherein said formulation is clear to the naked eye.
- 78. (New) The formulation of any of claims 1, 49, 66, 71, or 75 having an average particle size of from about 30 to about 75 nanometers.